Poster Session I

AUTOIMMUNE DISEASE

85
CD28 CONTROLS DIFFERENTIATION OF REGULATORY T CELLS FROM NAIVE CD4 T CELLS
Yu, X.-Z.[1,2], Guo, F.[1], Iclozan, C.[1], Suh, W.-K.[3], Anasetti, C.[1,2] [1] H. Lee Moffitt Cancer Center & Research Institute, Tampa, FL; [2] University of South Florida, Tampa, FL; [3] Institut de Recherches Cliniques de Montreal, Montreal, QC, Canada.

CD28 is required for the development of regulatory T cells (Tregs, CD4+CD25+Foxp3+) in the thymus and also contributes to their survival and homeostasis in the periphery. We studied whether and how CD28 and ICOS control the differentiation of Tregs from naive T cells. By using WT, CD28-, ICOS- or CD28/ICOS-knockout mice on C57BL/6 background as T-cell sources, we found that CD28 is essential, while ICOS is dispensable, for the development and homeostasis of Tregs as well as for the generation of Tregs from naive CD4+CD25- T cells in vivo. The requirement of CD28 for Treg differentiation was mediated by IL-2, because neutralization of IL-2 with its specific mAb blocked Treg differentiation from wild-type CD4+CD25- T cells and addition of IL-2 restored Treg differentiation from CD28-/- T cells. Other common γ-chain cytokines, IL-4, IL-7 or IL-15, do not share such a role of IL-2. However, a strong CD28-signal promotes expansion of T effector cells (CD25+Foxp3-) while inhibiting differentiation of Tregs. Our study demonstrates that CD28 delicately controls the process of Treg differentiation and T effector cell expansion in the periphery, which provides the "fine-tuning" of the balance between immune activation and suppression.

AUTOLOGOUS TRANSPLANTS

86
LONG-TERM FOLLOW-UP OF AUTOLOGOUS STEM CELL TRANSPLANT (ASCT) IN PATIENTS WITH MANTLE CELL LYMPHOMA (MCL)
Al-Farsi, K., Zadeh, S., Nagy, T., Franke, N., Keating, A., Crump, M., Kuruvilla, J. Princess Margaret Hospital, Toronto, ON, Canada.

Introduction: MCL is considered incurable with conventional therapy. ASCT has been shown to prolong progression free survival. However, reported median follow-up is generally short. We report a review of the outcome of patients (pts) with MCL who underwent ASCT at our institution with longer follow-up (f/u). **Method:** From May 1987 – Jul 2006, 47 pts underwent ASCT for advanced stage MCL, 43 of whom had adequate f/u data and were subsequently analyzed for outcome. **Results:** At ASCT, median age: 53 years (range 34–65), 36 males, CR: 21, PR: 22. 12 pts were transplanted beyond first CR or PR (>CR/PR1). Primary therapy: CHOP (n = 37; R-CHOP: 9) and other combination chemotherapy: 6. Salvage therapy in >CR/PR1: 7 had DHAP, 3 CHOP, 1 mini-BEAM and 1 ESHAP. 21 pts had rituximab before (11 with first line or salvage and 10 with mobilizing chemotherapy) and 11 had maintenance after ASCT. High dose regimen: CBV: 9, VP16/Melphalan/TBI 12Gy: 27 or VP16/Melphalan: 11. Stem cell source: peripheral blood: 40, bone marrow: 2 and mixed: 1. Progressive disease (PD) occurred in 21 pts; median time to progression post ASCT: 25 m. 32 pts remain alive (22 in CR, 10 have relapsed), while 11 pts have died of PD. No transplant related deaths. 4 pts developed secondary malignancies: 1 MDS, 1 skin (basal cell), 2 lung and 1 breast cancers. With a median f/u of 57 months from ASCT, median PFS was 42m while median OS has not been reached (5 year OS: 65%). Of pts who have not relapsed, 7 continue to be alive and disease free > 5 years after ASCT. Univariate analysis identified the use of rituximab before and/or after ASCT (p = 0.047) and ASCT in CR/PR1 (p = 0.001) as being statistically significant predictors of improved OS with only ASCT in CR/PR1 remained significant in multivariate analysis. For PFS, maintenance rituximab post-

ASCT (p = 0.03) and ASCT in CR/PR1 (p = 0.01) were significant on univariate analysis with ASCT in CR/PR1 remaining significant in the multivariate model (median PFS of 12m in >CR/PR1 vs. 62m in CR/PR1, p = 0.008). **Conclusion:** ASCT can achieve prolonged remissions in MCL with some pts having remission duration of over 5 years. Pts transplanted in first remission appear to have superior PFS and OS compared to those transplanted in later stages. Seconds cancers may be a concern with longer follow-up. A significant number of pts relapse after ASCT, necessitating the exploration of more effective treatment strategies such as the incorporation of rituximab before and/or after ASCT.

87
PERIPHERAL BLOOD STEM CELL TRANSPLANT FOR POEMS SYNDROME IS ASSOCIATED WITH HIGH RATES OF ENGRAFTMENT SYNDROME
Dispenzieri, A.[1], Lacy, M.Q.[1], Hayman, S.R.[1], Kumar, S.K.[1], Buadi, F.[1], Dingli, D.[1], Litzow, M.R.[1], Gastineau, D.A.[1], Inwards, D.J.[1], Elliott, M.A.[1], Micallef, I.N.[1], Ansell, S.M.[1], Hogan, W.J.[1], Porrata, L.F.[1], Johnston, P.B.[1], Afessa, B.[2], Bryce, A.[1], Kyle, R.A.[1], Gertz, M.A.[1] [1] Mayo Clinic, Rochester, MN; [2] Mayo Clinic, Rochester, MN.

Background: POEMS syndrome is a devastating syndrome, characterized by peripheral neuropathy, organomegaly, endocrinopathy, monoclonal plasma cells, skin changes, papilledema, volume overload, sclerotic bone lesions, thrombocytosis, and high VEGF. High-dose chemotherapy with autologous peripheral blood stem cell transplantation (ASCT) ultimately yields excellent clinical responses, but there can be considerable peri-transplant morbidity. **Methods:** Thirty patients with POEMS syndrome have been treated with PBSCT at the Mayo Clinic Rochester, 11 of whom have been previously reported. We retrospectively studied treatment outcomes, with an emphasis on treatment related morbidity. The definitions of engraftment syndrome (ES) used were of Spitzer (BMT, 27:893–8 2001) and Maiolino et al (BMT, 31:393–397, 2003). **Results:** Of the 30 patients, two-thirds were male. Median age was 48, range 20–60. The median time from the first symptoms and from the diagnosis of POEMS syndrome was 26 and 4 months, respectively. Patients had a median of 2 prior treatments (range 0–6). The median number of units of RBCs and apheresis platelets transfused were 6 and 5. During transplant period, patients had high rates of fever, diarrhea, weight gain, and rash (93%, 77%, 53%, and 43%, respectively). Only 13% remained outpatient, and median time to discharge from hospital was transplant day 17 (range 0–175). Factors that predicted for longer than median dismissal times included age (p = 0.04), abnormal chest radiograph 7 to 17 days post transplant (p < 0.0001), and bolus corticosteroids beyond day 12 post-transplant (p = 0.006). Splenomegaly was the baseline factor that best predicted for a complicated peri-transplant course.

	No Steroid (n = 16)	Steroid ≤ D12 (n = 7)	Steroid > D12 (n = 7)	P	P, early vs late CS
Weight change, %	0.6 (0.4.2–6.7)	6.7 (3.6–27.2)	11.2 (−2.1–23.2)	0.005	NS
Rash, %	27	71	43	NS	NS
Diarrhea, %	73	86	86	NS	NS
Tmax, °C	39 (37.8–41)	40.1 (39–41.1)	38.9 (38.7–40.8)	0.08	0.07
1st fever, day	10 (6–15)	8 (7–9)	12 (8–146)	0.007	0.007
Abnormal CXR1, %	13	71	71	0.03	NS
Ventilator, %	0	14	71	0.004	0.03
ANC500, day	15 (12–29)	16 (14–115)	18 (15–45)	0.08	NS
PLT20, day	12 (8–41)	20 (11–115)	24 (9–170)	0.05	NS
PLT50, day	15 (11–192)	32 (16–115)	56 (13–551)	0.03	NS
RBCs, units	3 (2–8)	6 (4–31)	11 (6–64)	0.0008	NS
PLTS, apheresis units	2 (1–9)	9 (4–51)	18 (4–60)	0.0004	NS
Hospital dismissal, day	15 (13–36)	21 (15–69)	41 (16–175)	0.009	0.05